COMPARATIVE EVALUATION OF VECURONIUM PANCURONIUM AND GALLAMINE ON CARDIOVASCULAR SYSTEM

THESIS

FOR

DOCTOR OF MEDICINE

(ANAESTHESIOLOGY)

BUNDELKHAND UNIVERSITY
JHANSI (U. P.)

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CERTIFICATE

Certified that the work entitled "COMPARATIVE EVALUATION OF VECURONIUM PANCURONIUM AND GALLAMINE ON CARDIOVASCULAR SYSTEM" which is being submitted as a thesis for M.D. (Anaesthesiology) was conducted by Dr. Mahendra Kumar himself in the department of Anaesthesiology, M.L.B. Medical College, Jhansi.

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This is to certify that the work pertaining to "COMPARATIVE EVALUATION OF VECURONIUM PANCURONIUM AND GALLAMINE ON CARDIOVASCULAR SYSTEM" which is being submitted as thesis for M.D.(Anaesthesiology) by Dr. MAHENDRA KUMAR has been carried out under my direct supervision and guidance in the department of Anaesthesiology.

The techniques and methods described were undertaken by the candidate himself and the observations recorded have been periodically, checked by me.

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A C K N O W L E D G E M E N T S

Word, in fact can not substitute for the feeling of gratitude, I have towards all who have helped me in this work.

There can be no greater opportunity than this to express my profound sense of gratitude to my esteemed and exalted guide and teacher Dr. A.K. Gurwara, M.S.,D.A., Reader in Department of Anaesthesiology, M.L.B. Medical College, Jhansi, who with his unfathomed knowledge and untiring zest for work guided me unflinchingly throughout this work. The present work has been possible because of his wise counsel, firm initiatives, timely and constructive criticism and valuable advice, which I have had the good fortune to receive.

I must express my deepest gratitude to my revered teacher Dr. P. Sahi, M.D.,D.A., Lecturer, Department of Anaesthesiology, M.L.B. Medical College, Jhansi, for his excellent guidance, supervision and unlimited help at every juncture, his constructive and meticulous suggestions have gone a long way in the accomplishment of this work.

I acknowledge with sincere thanks, the affectionate nature, heartening words and constant encouragement of Dr. U.C. Sharma, M.D.,D.A., Professor and Head of the Department of Anaesthesiology, M.L.B. Medical College, Jhansi, which has provided me the confidence and enthusiasm so essentially vital for successful accomplishment of such a study.

I am highly obliged and thankful to all of my senior staff especially -

1. Dr. D.D. Verma,
   M.D.,D.A.,
   Lecturer,
   Department of Anaesthesiology,
   M.L.B. Medical College, Jhansi.

2. Dr.(Mrs.) V. Gupta
   M.D.,D.A.
   Lecturer,
   Department of Anaesthesiology,
   M.L.B.Medical College, Jhansi.

who as a perpetual source of inspiration and knowledge bestowed upon me with remarkable generosity and benevolence.

I am highly obliged and thankful to our staff members of the Department of Anaesthesiology, whose encouragement and constant help make this work possible.

I shall always remain indebted to my parents, wife brothers and sisters for their unaccountable pain and sacrifice and their persistent inspiration which enable me to perform this work successfully. I most humbly take the liberty of dedicating this work to my parents.

I should appreciate the helping and co-operating attitude of my department workers - Mr. Zaheer Hasan (Clerk), Mr. Om Prakash (Technician) Mr. OM Prakash Yadav (department boy), Department of Anaesthesiology, M.L.B. Medical College, Jhansi, who helped me by all means time to time.

I am also thankful to Mr. K.C. Sharma for bringing out the work in representable form by his excellent ability of preparing type scripts.

Lastly, I am highly obliged to these patients who became the subjects of this work.

Date: 1.8.91

(MAHENDRA KUMAR)

C O N T E N T S

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INTRODUCTION

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Analgesia, Narcosis, and muscle relaxation constitutes the triad of requirements for general anaesthesia to provide satisfactory operative conditions. Ever since Griffith et al. used curare for clinical anaesthesia in 1942, newer muscle relaxants had been introduced from time to time with certain advantages over the existing muscle relaxants.

Neuromuscular blocking agents revolutionize the anaesthetic practice. It become possible to produce active muscular relaxation without unwanted depression of various systemes with the rapid advancement in the field of anaesthesiology. Muscle relaxants now have been used in millions of surgical patients for a variety of surgical procedures. However the muscle relaxants themselves have some undesirable side effects. The effect on heart and peripheral circulation occurs because of stimulation or inhibition of nicotinic receptors, in autonomic ganglia or on muscarinic receptors in the sinus node of the heart or as result of systemic histamine release. These autonomic action may result in changes in heart rate and rhythm, peripheral vascular resistance and venous capacitance.

However, suxamethonium has disadvantages limiting its use in certain situations. The accompanying rise in intragastric pressure, painful muscle stiffness due to fasiculation, hyperkalemia, cardiac arrthymias and even cardiac arrest have been reported with suxamethonium in burns and traumas cases (Mazze 1969). Breakdown products of suxamithonium tend to accumulate and have unwanted neuromuscular blocking property. These effects are not easily antagonised under these circumstances, use of a nondepolarising relaxants should be preferable for muscular relaxation which have a rapid onset and a relatively short duration of action.

The synthatic muscle relaxant gallamine triethiodide was first described in 1947 (Beret, Depierre and Lestrange) and introduced in to anaesthetic practice in the following year (Huguenard and Boul 1948). Although its primary action at the myoneural junction has been carefully evaluated. The occurence of circulatory changes following the use of gallamine triethiodide in anaesthesia was first reported in 1949 (Larmoureux Bourge Cavardin). These authors observed that tachycardia was an almost unvarying sequel to its

administration. It produced hypertension, increases cardiac out put and left ventricular work in anaesthetized humanse (Smith and Whitcher 1967). It is reported to produce ventricular arrathymias in 56% of patients who recieve the drug during cyclopropane anaesthesia (Wats and Prescott 1965). For producing complete aponea, it is used in the dose of 2mg/kg body weight by intravenous route, the duration of action is about 20-25 min. About 80% administered dose is excreted in kidney so should not be used in patients with renal disorders the remaining is antagonised by neostigmine and atropine.

One of the most fascinating contributions to medicine is the progress made in correlating chemical structure of drugs to their site and mode of action. Muscle relaxants represent a supreme example of success in this field. While investigating a series of aminosteroids, Hewitt and Savargein 1964 observed that when an acetylecholine like group was added to these triologically active compounds, some neuromuscular (N-M) blocking properties were obtained. One such compound, Pancuronium bromide appeared to be very effective (N-M) blocking agent without evidence

of any steroid activity. A large number of studies by various workers has resulted in the safe clinical introduction of this useful drug.

The Pancuronium bromide was clinically used in 1967 by Baired and Reed, and the advantages claimed were the absence of side effects, less histamine releasing activity (Loh 1970) and a weaker neuro-ganglion blocking action (Calton 1972). It did not appear to produced bronchospasm or hypotension, others worker have reported a rise in blood pressure (Loh 1970, Kelmann and Kennedy 1970).

There is a well recognized clinical need for new nondepolarizing relaxants of shorter duration, less cumulative propensity, and fewer side effects than presently available drugs. Now several new substances which do possess the desireble properties hypothetized above have been produced and are in various stages of clinical trial. These new relaxants will no doubt changes our patterns of practice by improving the safety and verstility of clinical relaxation.

Vecuronium is an excellent example of how an opparently minor molecular change may result in significant alteration of pharmacologic activity.

Chemically the drug is similary Pancuronium without the quaternizing methyl group in the 2-piperidine substitution (Pahey et al 1981), hence the trade name Nercuron. Vecuronium is therefore a Monoquaternary substance (although the tertiary amine at position-2 is probably protonated in the physiologic pH range). This seemingly minor chemical difference is responsible for all of the considerable pharmacologic differences between Vecuronium and Pancuronium. The absence of this methyl group reduces the acetyle-choline like character of the molecule in the area of ring "A" of the steroid nucleus, there by lessening its vagolytic propeoty without loss of neuromuscular blocking activity. Increased liver metabolic may be one reason for the shorter duration of action of Vecuronium compared to Pancuronium.

Vecuronium is one of several new relaxants currently undergoing clinical evaluation which appear to be actively metabolized within the body to relatively inactive derivatives. Vecuronium therefore have shorter duration of action and less cumulative effect than current drugs, as well as being less depends on the kidney for elimination (Agoston et al 1980, Marshall et al. 1980) and the residual is easily reveresed by Neostigmine.

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REVIEW OF LITERATURE

REVIEW OF LITERATURE

Kennedy et al. (1968) studied the cardiovascular effects of Gallamine triethiodide in 14 patients undergoing surgery. They observed that after Gallamine triethiodide, an increase in heart rate was found consistently. The tachycardia was marked both in degree and rapidity of onset. The average increase in heart rate was 40%. Tachycardia was said to occur however with small the dosage of Gallamine and has long been believed to result from blockade of the muscarinic effects of Acetylecholine librated from the post ganglionic vagal nerve endings. In this action the drug resembles atropine although it is much weaker (Laity and Garg 1962). There was no evidence of general sympathetic stimulation and the effect on preganglionic sympathetic nerves are minimal (Miller and Biscoe 1965). A direct stimulant effect on intra cardiac Beta receptores has recently been demonstrated but the extent to which the tachycardia results from this mechanism has not yet been decided. Elevation of Mean Arterial Pressure was found in all patients. The average increase in Mean Arterial Pressure was 13.80%. Blood pressure which differed significantly from the control Mean Arterial Pressure found at 1.3 and 5 minutes.

Loh (1970) observed the cardiovascular effects of Pancuronium bromide, compaired with d-tubocurarine in patients undergoing cardiac surgery. The pulse rate showed a slight rise with both drugs, but these changes were not statistically significant. It will be seen that there was a significant fall in systolic, diastolic and mean arterial pressure by 5 minutes after the injection of d-tubocurarine and that these tended to return towards control values at 10 minutes with Pancuronium there was a significant rise in arterial blood pressure by 5 minutes after injection of the drug. 10 minutes after injection the mean values remained above control values but were not statistically different from control.

John et al. (1971) compare the chronotropic effects of gallamine in man with that of atropine, in addition to correlate heart rate changes with degree of neuromuscular block over a wide range of gallamine dosages. They observed that gallamine produced tachycardia that was greatest at a dosage of 100mg regardless of the method of administration. Heart rate increased further when atropine 2mg was given after gallamine, indicating that gallamine does not produce complete vagolysis. The magnitude of

tachycardia with gallamine was much less than that following atropine in either incremental doses of 0.2mg/kg. body weight or a single bolus dose of 2.0mg/kg. body weight suggesting that gallamine may not act in the same manner as atropine.

Kelman et al. (1971) investigated the effects of Pancuronium bromide (0.07mg/kg. body weight) on heart rate, mean arterial blood pressure, Cardiac out put and calculated total peripheral resistance in ten artificially ventilated patients anaesthetized with 60% N_2O in oxygen and phenoperidine (1mg/15kg body weight). According to their observation, Pancuronium caused a marked increase of heart rate (22-26%) and of mean arterial blood pressure (5-7%). These changes were all statistically significant.

Robert K. Stelting (1973) observed that gallamine (1 and 2mg/kg) produced sustained increases in heart rate for at least 20 minutes. The maximum increases were nearly same after 1 and 2mg/kg of gallamine, suggesting that the degree of tachycardia was independent of the dose used. This agrees with the study of Eisele et al (1971), who reported maximum tachycardia after 50-100mg of gallamine, mean arterial

pressure increased slightly after 1 or 2mg/kg of gallamine.

Bhatia et al. (1975) was observed that Pancuronium causes slight rise in pulse rate or no change at all. Whereas with d-tubocuranine, there was decrease in pulse rate or no change. Rise in systolic blood pressure (36% of the cases) or no change was observed with Pancuronium, on the other hand fall in systolic blood pressure (36% of cases) or no change was observed with d-tubocuranine.

Dhanaraj et al. (1976) observed that there was no fall of blood pressure with Pancuronium, on the other hand systolic blood pressure increased in all cases. There was a fall in systolic blood pressure of about 11.53mm of Hg (range 4-40mm of Hg) but the pulse rate was slightly increased, whereas with gallamine, there was increased in pulse rate and no change in blood pressure.

A comparative study of the cardiovascular effects of Pancuronium bromide with d-tubocuranine chloride in anaesthetized patient was done by Mrs. Bhargwa et al. (1978). They concluded that in 84% of patients there was no any change in pulse rate. The rise in pulse rate of about 0 to 10 per minute in 12% of the patients and 11 to 20 per minute in 4% of patients was observed. They were also observed that

no change in blood pressure in 20% of patients. Rise in blood pressure ranging from 0 to 10mm Hg in 40% of patients, 11 to 20mm of Hg in 20% of patients, 21 to 30mm of Hg in 12% patients, 31 to 40mm of Hg in 4% of patients and 50 to 60mm of Hg in 4% of patients. Thus Pancuronium produced rise in blood pressure in 80% of patients. On the other hand the pulse rate and blood pressure both were decreased with d-tubocuronine.

The effects of Pancuronium was studied by Singh (1979) in 50 adult patients, repeated observations were made of sytolic blood pressure and pulse rate. Maximum changes in blood pressure associated with Pancuronium were noted over the base line level i.e. before induction of anaesthesia. As all the cases were given halothane which has got the property of causing hypotension and bradycardia and this fact was kept in mind. In 48% cases there was slight rise of blood pressure while in 38% canes there was moderate rise in blood pressure. In 10% cases there was a severe rise in blood pressure. There was no rise in diastolic blood pressure which remained within normal limit. Maximum changes in pulse rate associated with Pancuronium

were recorded. In 90% cases there was tachycardia. In 72% cases there was slight tachycardia while in 8% cases there was moderate tachycardia. In 10% of cases there was bradycardia but it was within normal limits.

According to Savarese et al. (1979) Gallamine and Pancuronium produced increase in heart rate in man principally by blocking vagal muscarinic receptors in the sinus node of the heart (Hughes et al. 1979). Both these drugs may also have indirect sympathomimetic effect. A rise in arterial pressure of 10-20mm Hg following the administration of Pancuronium and Gallamine is common (Stoelting R.K. 1973).

Gupta et al. (1980) evaluates Pancuronium bromide on different clinical parameteres in relation to gallamine triethodide and d-tubocuramue-hydrochloride. They observed that all the three muscle relaxants raised the pulse rate but, the increase in pulse rate was not significant with Pancuronium and d-tubocurarine. There was however a significant rise in pulse rate with gallamine triethiodide. Pancuronium bromide and gallamine tristhiodide caused minimal changes in blood pressure while d-tubocurarine caused hypotension in all most all the cases. The mechanism of action of

Pancuronium or Gallamine on blood pressure is through the cardiac vagus in animal, in a manner similar to atropine. This is supposed to be the probable cause in man also. Hypotension with tubocurarine in thought to be due to histamine release and ganglionic blocking property, which is absent or minimal in Pancuronium.

Daksha et al. (1980) clinically compared Pancuronium, with Tubocurarine and Gallamine. They were found that tubocurarine has a definite hypotensive effect. Gallamine caused lesser fall in B.P. in some cases and a slight rise in others, while Pancuronium caused no fall in B.P. and in some cases there was a slight rise. Pulse rate was found to be reduced or consistent with tubocurarine, increase after Gallamine and raised or consistent with Pancuronium. The same is confirmed by several published reports of workers in the past. Hypotension caused by tubocurarine is due to Ganglionic blockade and histamine release. Hypertension following Gallamine could be due to vagal blocking action causing tachycardia and also a direct stimulating effect on intracardiac beta receptores. Hypertension and tachycardia following Pancuronium is could be due to vagolytic and release of catecholamines.

Sheth et al. (1980) compare the cardiovascular effects of Pancuronium bromide with d-tubocurarine and Gallamine. They observed that there was no change in pulse rate in 60% patients with Pancuronium, 8% had a decline while 32% showed a rise. The mean rise was 3.62 beats per minute. The mean rise in pulse rate for d-tubocurarine and Gallamine was 1-20 beat per minute and 10-92 beat per minute respectively. There was no difference due to first or second dose. The rise in pulse rate with Pancuronium is a constant finding reported by many authors. Komesaroff (1970) has noted that a rise in pulse rate was observed in case where the initial pulse rate was low but little change was observed in these cases whose initial pulse was high, a situation which is more likely to rise in emergency operations or condition like thyrotoxicosis and mitral stenosis where by any further rise in the already high pulse rate would be disastrous. There was no change observed in blood pressure in 40% of cases with Pancuronium, 4% had a decline while devation of blood pressure was observed in 56%. The mean rise was 5.40mm of Hg. With d-tubocurarine there was a mean fall of 9.60mm of Hg and with Gallamine a

mean rise of 6.76mm of Hg. There was no difference due to first or second dose. It has been observed that when N_2O-O_2 and fantanyl were used as maintance anaesthatic, the fall in blood pressure was significantly greater with d-tubocurarine than with Pancuronium, when halothane was substituted for fentanyl, d-tubocurarine produced a significant fall in blood pressure while Pancuronium did not produced a clinically significant change of blood pressure.

Org NC 45 caused no significant cardiovascular changes, Pancuronium increased heart rate, mean arterial blood pressure cardiac out put and pulmonary wedge pressure and it decreased systemic vascular resistance ($P<0.05$). Although metocurine also increased heart rate and cardiac out put ($P<0.05$) mean arterial blood preasure and pulmonary wedge pressure did not change d-tubocurine decreased all cardiovascular parameter except heart rate which increased significantly (Booij et al. 1980).

According to Crul and Booij 1980, no changes in arterial pressure and heart rate occured after giving Org NC 45 even in doses of up to three times the 95% blocking dose where as some degree of tachycardia and and an increase in arterial pressure were usually seen

after giving Pancuronium.

Joshi et al. (1981) clinically compared Pancuronium bromide, Gallamine and d-tubocurarine in 150 cases. They observed that there was rise in blood pressure in 40% of patients with Pancuronium bromide. The rise in blood pressure ranging from 0 to 10mm of Hg in 32% of patients 10-20mm of Hg in 6% of patients and 20-30mm of Hg in 2% of patients, with Gallamine, rise in blood pressure was observed in 48% of patients. There was no changes in blood pressure in 46% of patients with Pancuronium and 36% of patients with Gallamine. This rise in blood pressure caused by Pancuronium and Gallamine was not clinically significant. Rise in pulse rate was maximum (84%) with Gallamine. The range was 0-10 beats in 22%, 10-20% beates in 38%, 20-30 beats in 16% and 30-40 beats in 8%. With Pancuronium, rise in pulse rate was observed in 64% of patients. The range was 0-10 beats in 40% patients, 10-20 in 16% of patients, 20-30 beats in 2% of patients. There was no change in pulse rate was observed in 28% of patients with Pancuronium and 14% of patient with Gallamine. This rise in pulse rate was not clinically significant. Comparing these results, Pancuronium provided a better cardiovascular stability.

Administration of Org NC 45 minimal changes in the heart rate and blood pressure during the subsequent 10 minute in patients anaesthetized with Halothane or Englurane on the other hand, Pancuronium always increases the heart rate, Systolic and Diastolic blood pressure increased constantly but minimally after Pancuronium in patients anaesthitized with Halothane, whereas they did not change in patients anaesthetized with enflurane. Sergio et al. (1982).

A comparative study of Org NC 45 and Pancuronium on heart rate and arterial pressure in anaesthetized man was done by Barnes et al. (1982). They observed that the effect of bolus dose of Org NC 45 on heart rate in lightly anaesthetized man is different from that Pancuronium. The dose of Org NC 45 used in this trial appears to be devoid of the vagal blocking action observed with Pancuronium. Animal studies which have shown Org NC 45 to be devoid of vagal blocking activity (Booij et al 1980, Durant, Heuwerttes and Crul 1980) have conferred in man. The changes observed with Pancuronium are consistent with previously reported work (Kelman and Kennedy 1971, Miller, Eger and Stevens 1975) when Pancuronium is used in clinical practice, a stimulus that produces a sympathetic discharge result

in tachycardia that would be more marked in the presence of vagal blockade. Excessive tachycardia may occure when Pancuronium is used this would be less likely to occur with, Org NC 45. The effect of Pancuronium and Org NC 45 on mean arterial pressure to be dependent on the conditions prevailing at the time the data were collected. Org NC 45 did not have a consistant effect on mean arterial pressure after a bolus injection in the lightly anaesthetic used unstimulated subject, and changes that did occur were minimal. The injection of Pancuronium resulted in a small but significant increase in arterial pressure. This increase in mean arterial pressure did not appear to correlate with the increase in heart rate. The increase in mean arterial pressure during intubation after Org NC 45 was modest and consistant. The increase in mean arterial pressure in those patient who had received Pancuronium was greater and tended to inconsistant.

In clinical studies on Org NC 45 comparison with Pancuronium, by Karr et al. (1982). The heart rate and arterial systolic pressure changes for the first 30 minutes following injection of the intubating

dose of each drug. At 15 minutes following injection of Org NC 45 and when the surgical stimulus was absent or minimal there was no evidence of tachycardia, this agrees with the findings from other clinical studies of this drug. Animal experiments have shown that in contrast for Pancuronium and other nondepolarizing muscle relaxants Org NC 45 in doses 20 times greater than those required for neuromuscular blockade, has no effect on the heart rate, arterial pressure or the sympathetic nervous system (Marshall et al. 1980).

Cardiovascular effects of Org NC 45 and Pancuronium were examined in seven anaesthetized dogs by S. Titzal et al. in 1983. They found that equipotent doses of Org NC 45 (0.025mg/kg) and Pancuronium (0.03mg/kg). Heart rate increased significantly from 104.5±9.9 to 121.1±8.6 beat per minute after Pancuronium ($P<0.05$) whereas Org NC 45 has no effect. Neither drug had any effect on systolic diastolic or mean arterial pressure. Tachycardia observed in their study after I.V. administration of Pancuronium was dose related. No increase in heart rate was found by Miller and colleagues (1975) nor was it reported in the experimental study Demenoch and colleagues (1976), it was however describe in a clinical investigation by Parmentair and Dagnetie (1979). Org NC 45 irrespective of dose and type of application did not induce any changes in heart rate or systemic

pressure. Thus Org MC 45 administered in clinical doses does not induce any vagalytic activity. Moreover, there was no evidence of direct inotropic action on myocardium.

Engback et al. (1983) observed the cardiac effects of Vecuronium and Pancuronium during Halothane anaesthesia in 20 adult female patients scheduled for gynaecological operation. According to their observations, Pancuronium 0.08mg/kg caused increased of 20% heart rate after 1 minute. Heart rate remained unchained for the following 10 minutes and was significantly greater during the first 5 minute compared with the group receiving Vecuronium. An increase in mean arterial pressure of 8% was seen one minute after the injection of Pancuronium. Vecuronium 0.057mg/kg caused no changes in heart rate and no significant changes in mean arterial pressure.

The cardiovascular effects of Vecuronium bromide and Pancuronium bromide were compared by Bhatia and Mrs. Dave (1985) in 50 patients between the age of 40 to 60 years scheduled at for elective major cancer surgery. They observed pulse rate for first five minutes and then up to 15 minutes, shows

that there is no change in 60% to 72% of cases with Vecuronium while with Pancuronium there is definite tachycardia in all patients. Robert B. Morries et al. (1983) observed the same effects, may stated that tachycardia produced with Pancuronium are due to its vagolytic and sympathonimatic properties. While Org NC 45 being devoid of autonomic neural activities. It does not produced any cardiovascular effects (Gregoretti et al. 1982). Gallamine causes atropine like response and produces tachycardia and Pancuronium produces similar effects although responses is less profound. They also noticed changes in arterial systolic blood pressure during first five minutes and up to 15 minutes. The observation shows that with Vecuronium there was no change in B.P. in 44% to 68% of cases while with Pancuronium 96% to 98% of cases there was increase in Blood Pressure. Moris et al. observed that pulse rate and mean arterial blood pressure did not changes following Vecuronium, while increased 22% and 24% respectively following Pancuronium.

The effect of Atracurium, Vecuronium and Pancuronium on heart rate and arterial blood pressure in normal individuals were studied by Lavery et al. (1986). Heart rate and rhythem (from ECG) and systolic,

diastolic, and mean arterial pressure (using an ease-illotenometer) were measured for 30 minutes following administration of atracurium 0.5mg kg^{-1}, Vecuronium 8mg kg^{-1} or Pancuronium 0.1mg kg^{-1} during steady - state anaesthesia, with nitrous oxide, oxygen and either 0.75% halothane or fentanyl 4-5 ug kg^{-1}. With halothane anaesthesia Atracurium causes only minimal changes in Heart rate, Systolic arterial pressure, Mean arterial pressure, Diastolic arterial pressure, although these were statistically significant at times. The Heart rate changes after Vecuronium were minimal (a maximal fall of 7bPM or about 9%). Changes were significant ($P<0.05$) at 1 and 30 minutes. There was significant fall ($P<0.05$) in Systolic arterial pressure and Mean arterial pressure (up to 15 and 19% respectively) during the period 3-15 minutes after administration of Vecuronium. Diastolic arterial pressure showed a significant decrease ($P<0.05$) throughout the 30 minute period. Heart rate after administration of Pancuronium was significantly increase ($P<0.01$) within 1 minute and remained so ($P<0.001$) at every subsequent observation. There were no significant changes in Systolic or Diastolic arterial pressure but Mean arterial pressure rose significantly ($P<0.01$) in the 3 minutes after administration of Pancuronium

with fentanyl anaesthesia. Atracurium produced gradual reduction in Heart rate, becoming significant ($P<0.05$) of the 20,25, and 30 minutes observations when the decrease was of the order of 5-6%. Three to five minutes after administration of Atracurium, Systolic arterial pressure, Diastolic pressure and Mean arterial pressure were decreased significantly ($P<0.05$) but from that point arterial pressure began to increases and by 25-30 minutes was significantly greater ($P<0.05$) than the control. The Vecuronium showed no significant changes in Heart rate. Arterial pressure showed significant reduction ($P<0.05$) 3-5 minutes after Vecuronium administration. However by 30 minutes, Diastolic arterial was significantly greater ($P<0.05$) than the control. Heart rate after Pancuronium had significantly increased ($P<0.01$) at 1 minute and remained as ($P<0.001$) up to and including, the 30 minutes observation. Systolic arterial pressure significantly increased at 5,15, 20 and 30 minutes. Diastolic arterial pressure and Mean arterial pressure were increased from 1 to 30 minutes after Pancuronium administration.

Singh et al. (1987) observed the comparative effects of Pancuronium and d-tubocurarine in major abdominal surgery. They concluded that Pancuronium

produced a rise in systolic pressure in 88% cases while in 12% cases there was no change. Tachycardia was observed in 4% cases, the other 16% cases had no change in heart rate.

According to Mrs. Jana et al. (1988) Vecuronium did not produced any clinically important effect on the pulse rate and systolic blood pressure although intubation after Vecuronium did cause a significant rise in pulse rate any systolic blood pressure. These cardiovascular effects were similar to those reported by Morries et al. (1983).

Agarwal et al. (1989) was clinically compaired the Vecuronium with Pancuronium and observed that mean pulse rate and mean arterial blood pressure were elevated to a highly significant level during intubation which satteled after about 10 minutes to a level above the preinduction level with both drugs, but rise in pulse rate and mean arterial blood pressure was significantly less ($P<.001$) with Vecuronium as compared to pancuronium both during intubation and after 10 minutes of injection of muscle relevants. This is in conformity with the views of Barner et al. (1982). Mild tachycardia and slight rise in Mean arterial pressure after 10 minutes of injection of Vecuronium

may be because of light plane of anaesthesia in this study since no other narcotic or inhalational agent other than N_2O was used. So they concluded that Vecuronium bromide had better cardiovascular stability as compared to Pancuronium.

Cardiovascular effects of atracurium besylate and Pancurium were compared (Singh et al. 1990). They found that patients receiving Pancuronium showed significantly higher mean pulse rates 5 and 10 minutes after this relaxant. The second dose of Pancuronium also resulted in significantly higher pulse rate 5 minutes after it. The mean arterial blood pressure 10 minutes after the initial dose of Pancuronium was significantly higher than the corresponding mean value of atracurium. The mean arterial pressure after the second doses of the two relaxant were comparable.

Baijal et al. (1990) clinically compaired the Pancuronium, Vecuronium and Atracurium. They observed that a significant increases in pulse rate was seen in patients receiving Pancuronium. With Vecuronium there was an initial rise followed by fall in pulse rate. In patients who received atracurium showed a slight fall in pulse rate. Patients receiving

Pancuronium showed a significant increase in mean arterial pressure while patients receiving Vecuronium or Atracurium exhibited a stable blood pressure without much rise or fall even after intubation.

Muralidhar et al. (1990) compare the Vecuronium and Pancuronium during surgical treatment of patant ductus arteriosus. They observed that the heart rate in patients receiving Pancuronium were significantly increases ($P<0.05$) from 119.1±12.4 and 122.7±9.9 after the administration of the relaxant and after endotrachial intubation respectively. In patients receiving Vecuronium there was no significant changes in the heart rate at these events. The systolic blood pressure with Pancuronium rose significantly from a preinduction value of 116.0±16.2mm Hg to 130.7±12.4mm Hg and 130.0±11.4mm Hg after the administration of the relaxant and after endotrachial intubation respectively. The systolic blood pressure with Vecuronium fall slightly but significantly from a preinduction value of 121.0±15.1mm Hg to 114.7±10.1mm of Hg after the administration of relaxant but rose back to the control value after the endotrachial intubation. There was no significant change in diastolic blood pressure after relaxant administration and endotrachial intubation in patients receiving Vecuronium. Whereas there was a significant

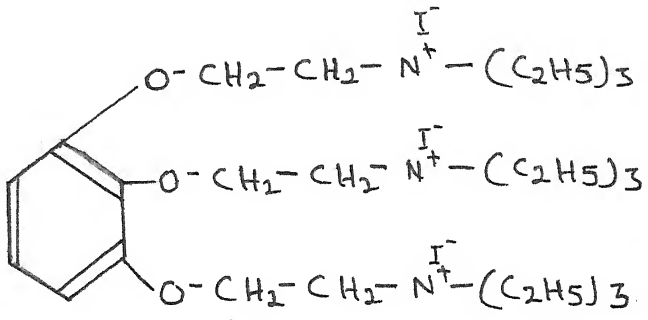
increases in the diastolic blood pressure in patients receiving Pancuronium when the preinduction value was compared to the post relaxant and post intubation values.

Singh et al. (1990) compared the cardiovascular effect of Atracurium and Pancuronium. They observed that Pancuronium showed significant higher pulse rates 5 and 10 minutes after this relaxant. The second dose of Pancuronium also resulted in significantly higher mean pulse rate 5 minutes after it. The mean arterial pressure 10 minutes after the initial dose of Pancuronium was significantly higher than the corresponding mean value with Atracurium.

GALLAMINE TRIETHIODIDE

In 1947, Bovet and his coworkers describe a synthetic muscle relaxant gallamine triethiodide. The effects of this relaxant in man were first described by Huguendard and Boue (1948) in France and by Mushin and his colleagues (1949) in England.

Gallamine triethiodide in chemically tri (B-diethylaminoethoxy) - Benzine trithiodide. It is white amorphous powder, nonirritant, relatively stable and available in 40mg/ml solution in 2ml and 10ml ampules.



STRUCTURAL FORMULA OF GALLAMINE TRIETHIODIDE

The intravenous bolus of Gallamine triethiodide (1.5-2mg/kg) is the most prefered rout with the average dose of 100-140mg for total cessation of respiration and muscular relaxation. The onset of action occurs within 90-120 second and duration of action between 20-30 minutes, when injected subcutaneously the activity is about one

quarter that of an intravenous injection. It is inactive by months. Supplementary doses of gallamine 20-40mg are given as required.

Gallamine triethiodide acts at the neuromuscular junction by nondepolarization block. The curare molecule combines with the end plat. receptors and this denies the acetylcholine molecule access to its norwal destination.

Gallamine distributed throughout the body and about 30-100 percent is excreted unchanged in urine within two houres (Mushin et al. 1949). Prelonged paresis may follow the use of gallamine in cases with poor renal function. (Fairley 1950, Montgomery and Bennett-Jones 1956, Feldman and Levi 1963). This is partly due to loss of redistribution sites in the kidney and also due to the lack of alternative path ways of excretion for the drug (Feldman et al. 1969). It is bound to serum albumin and the increase in potency by increasing the pH. Sensitivity occures in myesthenia grevis and in the presence of anaesthetics with a curare like action such as ether.

Gallamine produced tachycardia in man by blocking the vagal muscarinic receptores in the sinus

node of the heart Brown et al. 1970 and by indirect sympathemimalic effects. The tachycardia in man is dose dependent to gallamine, reaching a maximum at 1mg/kg. 100% heart rate may increases if the patients base line rate was slow, Gallamine is strongly vagolytic in the neuromuscular blocking dose range, often resulting in heart rate of 90 to 120 beats per minute in the presence of adequate neuromuscular blockade.

A rise in arteriel pressure of 10 to 20mm Hg following the administration of Gallamine is common (Stoelting 1973) in the absence of potent anaesthetic. Increased heart rate secondary to the vagolytic effect of this drug in the absence of any fall in peripheral resistance is the probable mechanism involved.

Gallamine have been produce weak positive inotropic effects in cardiac muscle (Brown et al. 1970). Release of catecholamine may be increased within the heart or relative shift of autonomic tone to the adrenergic side in the heart due to cardiac muscarinic receptor block.

In normal man Gallamine increase cardiac out put without any important change in peripheral resistance.

Cardiac out put increases in the range of 25 to 53% after 0.5 to 2.0mg per kilogram given as a bolus intravenously and sustained for 5 to 20 minutes.

Arrhythmics after administration of gallamine may occur as a result of:

(1) Suddan shift of autonomic balance toward the adrenergic side due to the vagal-blocking effect the drug (Brown et al.1970).

(2) A possible sympathomimatic effect.

(3) A relatively great inhibition of the atrioventricular node than the sinus node. These mechanisms may be manifest clinically as single or multifocal premature ventricular contractions or ventricular tachycardia or nodal tachycardia under light halothane or cyclopropane anaesthesia. In known sinus nodal disease, a vagolytic effect might cause a relatively greater increase in the spontanious rate of activity of the atrioventricular node than the sinus node, result is nodal tachycardia.

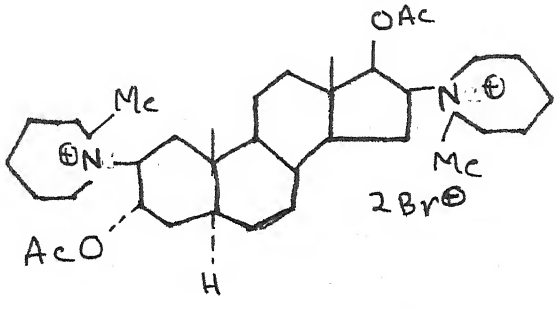
Gallamine inhibit muscarinic receptores this action is an atropine like effect and is limited to cardiac receptores. There is no effect on bowel, salivary glands, pupil or other muscarinically inervated end organs. Experimentally, both vagal induced bradycardia and bradycardia secondary to acetylcholine or methacholine are blocked (Hughes et al. 1976).

There is no evidence available to suggest that gallamine has any action on the central nervous system in man. It has no any direct action on liver and kidney. Indirectly, however, it has a weak inhibitory effect on the plasma cholenesterase produced by the liver.

PANCURONIUM BROMIDE

Pancuronium bromide was introduced in clinical anaesthesia by Baired and Reid in 1967. It is a odurless, while crystaline powder with a bitter test, it melts at 215°C with decompositon.

Chemically Pancuronium bromide is a bis-quaternary ammonium compound which is relatively stable and is supplied for clinical purposes in 2ml ampules containing 2mg/ml.



CHEMICAL STRUCTURE OF PANCURONIUM

The intravenous bolus of Pancuronium (0.08 to 0.1mg) is the most prefered route with the average intubation dose 5 to 8mg. onset of paralysis occur within 1.5 to 3 minutes. The paresis produced by Pancurenium last for about 25 to 45 minutes and a satisfactory "topping up dose" is about 1/5 to 1/10 of the original paralysing dose.

Pancuronium acts at the neuromuscular junction in man by non-depolarisation (Baird and Reid 1967).

Pancuronium is believed to be excreted mainly unchanged in the urine, but can be biodegraded to less active and inactive compound by metabolism of the 3 and 17 acetyl groups of the parent compound. Up to 15% of an injected dose of Pancuronium may be recovered from urine as 3-hydroxy derivative. In the absence of renal excretion large amount of the drug can be recoved from the bile much in the form of steroids in which the or 17 acetyl group has been hydrolysed to either the hydrogen or hydroxy derivative.

Like all the muscle relaxants it is a highly charged ion and is therefore unlikely to pass vital membranes easily. There is no evidence available in man that it is not believed to cross blood brain barrier.

It possesses very little fat solubility.

Pancuronium has little effect on the cardiovascular system(Baird and Reid 1967, Levin et al. 1971). There is little changes in pulse rate in doses less than 0.06mg/kg although some vagolytic activity occures at higher dose levels. It has been suggested that Pancuronium may tend to produced an increase in blood pressure by sympathetic stimulation, especially in the presence of autonomic irritability. Evidence suggested that Pancuronium produced a direct but short lived inotropic effect upon the intact heart. It increases the peripheral resistance. Because of the absence of hypotension this drug is preferred for patients with cardiovascular instability and in low out put states.

There was no evidence suggested histamine release after administration of Pancuronium. This is believed to account for the absence of both hypotension and bronchospasm following its use: however allergic reactions have been reported (M.C-dowell and Clark 1969, Nama et al. 1972).

Pancuronium can be easily reversed by neostigmine in the usual manner. Pancuronium is a weak inhibitor of

plasma cholinesterase, but some of its metabolic derivatives are more active in this respect.

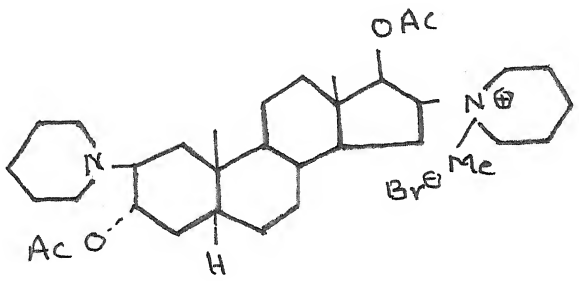
VECURONIUM BROMIDE

Vecuronium bromide was originally known by its research code ORG NC 45 and was developed by Dr. David Savage of organon Technika laboratories (Savage et al. 1980). Vecuronium was developed by non hormonal properties of steroid molecule, which is an androstanyl derivative of acetylcholine.

Vecuronium bromide is a buffered freeze-dried powder, available as 4mg per ampoule, with 1ml ampoule of water for injection as solvent. The ampoule of powder can be kept for 3 years provided they are stored in the dark at a temperature below 25°C.

The trade name of Vecuronium, Norcuron, reflects the fact that 'nor' indicates, that Vecuronium has exactly the same chemical structure as Pancuronium except for the absence of a methyle group. The missing methyle group is the one which is attached to the quaternary nitrogen atom which is itself attached to the A ring of the steroid neucleus. Vecuronium is

a Monoquaternary homologue of Pancuronium, having negligible ganglion blocking and vagolytic properties (Agoston et al. 1980).



CHEMICAL FORMULA OF VECURONIUM

Vecuronium in the dose of 0.1mg/kg have been reported to produce excellent to good intubating condition in 90 seconds (Nirbhur et al. 1983). Large doses of Vecuronium (0.15 to 0.2mg/kg) improve intubating condition at 1 minute after their administration, such

that at least 60% of patient can be regarded as excellent and after 90 seconds produces such condition in 90-95% subjects and at this time there is no difference whether 0.1mg/kg of Vecuronium or twice of this amount has been given. Intubation is unlikely to be smooth or may not even succeed with doses below 0.25mg of Vecuronium despite waiting for adequate time after administration.

The maintanance dose of Vecuronium is 0.03 to 0.05mg/kg body weight. The duration of effect is 10-20 minutes. However the larger doses of Vecuronium could lead to a prolonged total duration of action. It is metabolise in the liver and mainly excreted in the bile, a small quantity is also excreted in the urine.

Children are more resistant to its effects than adolescents. The duration of effect after 0.07mg/kg was 73 minutes thus Vecuronium has a larger volume of distribution in infants and children than in adolescents and adults.

The neuromuscular effects of Vecuronium are potentiated by both respiratory and metabolic acidosis. The alkaline medium accelarates the decomposition of Vecuronium. The potentiating effects of hyperventilation on the duration of neuromuscular block are probably minimal in clinical practice.

Clinical degree of hypercapnia or hypokapnia established after but not before the administration of Vecuronium are associated with changes in twitch tension compared with normocapnic condition. An increase in arterial PCo_2 is associated with a decrease in twich tension and vice versa.

The cumulative effects was not seen after repeated doses of Vecuronium.

Vecuronium is devoid of significant influence on heart rate and arterial pressure (Fahey et al. 1981, Savage et al. 1980) and their lack of sympathetic stimulation and vagal-blocking effect make them superior to gallamine, Pancuronium and fazadinium (Engbeak et al. 1983). In vitro tissue preparation show that Vecuronium possesses an antimuscarinic action 1-3 times less than Pancuronium.

Vecuronium shows excellent tendencies towards spontaneous recovery of neuromuscular function without necessarily involving the need for a specific antidote. Antagonism of the neuromuscular block produced by Vecuronium can be achieved with anticholinesterases such as neostigmine in the dose of 0.04 to 0.08mg/kg body weight with 1.2mg of atropine (Marshall et al. 1980).

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MATERIAL AND METHOD

MATERIAL AND METHODS

The present study was conducted in the department of Anaesthesiology in M.L.B. Medical College and Hospital Jhansi (U.P.) during year 1990-1991, with the aim to compare and evaluate the effects of Vecuronium, Pancuronium and Gallamine over the cardiovascular system.

Ninty adult, indoor patients of either sex between 20 to 65 years of age scheduled for various elective surgical procedures, requiring trachial intubation and muscular relxaion under general anaesthesia, comparized the material for study. Patients were divided in to three groups of 30 each. Each group was given one particular relaxant during anaesthesia. Patients having any Renal, Hepatic or Cardiovascular disease were excluded from the study.

All the patients were physical status as A.S.A. grade I or II. They were throughly examined preoperatively to the clinical fitness. Routine investigations along with relevant special investigation were performed in all the patients, only patients with normal investigations were accepted for the purpose of study. An informed written

consent was obtained from every selected patient, and they were kept empty stomach for at least 6 hours before the induction of anaesthesia.

Premedication consist of injection atropine 0.6mg and injection diazepam 10mg both intramuscularly, 30-45 minutes prior to the induction of anaesthesia.

Venepuncture was performed with a 16 or 18 gauze I.V. Cannula under proper aseptic condition. A 5% Dextrose in D/W was started, pulse, systolic and diastolic blood pressure were recorded two minute prior the induction of anaesthesia to serve as a base line records.

Pre-oxygenation with 100% oxygen was initiated 3-5 minutes prior to the induction. Induction of anaesthesia was performed with the sleeping dose (4 to 6mg per kg body weight) of 2.5% Thiopentone Sodium slowely, till abolition of eye lash reflex. Intubation was done by proper size cuffed endotracheal tube with Suxamethonium in the dose of 1.5 to 2mg per kg body weight (80-100mg), connection were made to attach the patient with the Mapleson A circute of Boyel's Apparatus. I.P.P.V. was continued.

When the effect of suxamethonium completely were out the chosen nondepolarizing muscle relaxant administered in the following manner.

GROUP-I (Vecuronium group) 30 patients

All these patients received Vecuronium in the doses of 0.08mg per kg body weight intravenously.

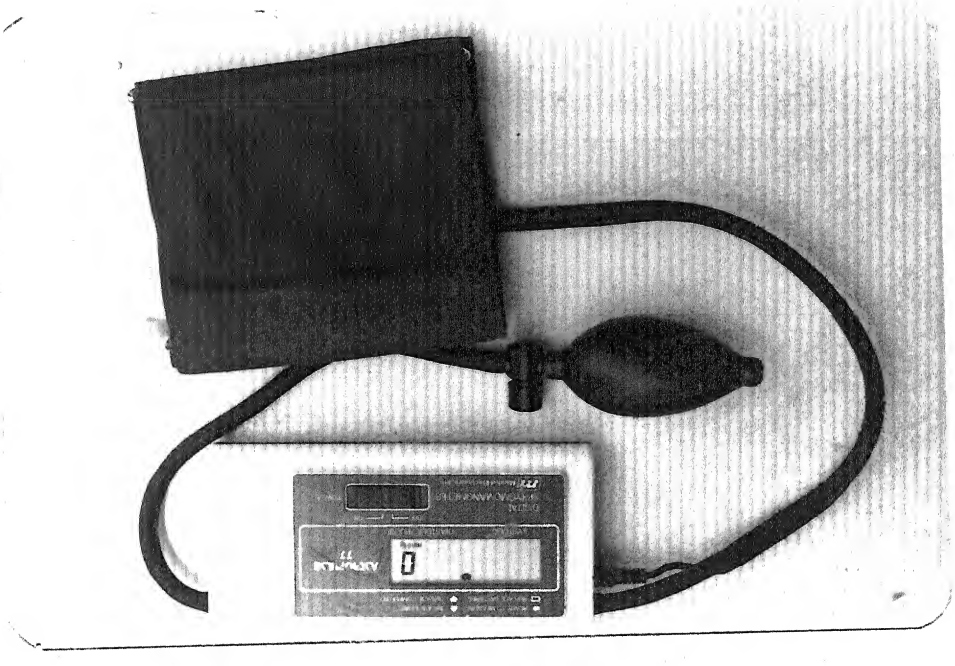
GROUP-II (Pancuronium Bromide) 30 patients

All these patients received Pancuronium in the doses of 0.1mg per kg body weight intravenously.

GROUP-III (Gallamine Triethiodide) 30 patients

All these patients received gallamine in the doses of 2mg per kg body weight intravenously.

Anaesthesia was maintained with nitrous oxide and oxygen (65:35) I.P.P.V. was carried out but hyper- or hypoventitation was avoided. Supplemental doses of Pethidine were given to maintain analgesia during surgery. No other volatile inhalational anaesthetic was used during the procedure. Incremental dosage of muscle relaxants were given in the dose Vecuronium 0.02mg per kg body weight, Pancuronium 0.02mg per kg body weight, as and when required.



ASTROPULSE 77
(digital sphygmomanometer)

Pulse, systolic blood pressure and diastolic blood pressure were recorded. Pulse and blood pressure were recorded with Astropulse 77 (digital sphygmomanometer) every 5 minutes after giving the muscle relaxants.

At the end of surgery, and return of flickering movements in the rebreathing bag the residual relaxants were antagonised with 1.2mg Atropine and 2.5mg Neostigmine intravenously. Patients were extubated after establishment of spontaneous respiration. Suction was done for clearing the oral cavity from secretion just before extubation and after extubation. Patients were oxygenated with 100 percent oxygen for 5 to 10 minutes after extubation. Post operative pulse rate and blood pressure were recorded.

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OBSERVATION

OBSERVATION

In the present study the effects of Vecuronium, Pancuronium and Gallamine were compared and evaluated on cardiovascular system in 90 patients. The patients were of both sexes and over the age of 26 years but below the age of 65 years.

These ninety patients were randomly allocated in to three groups depending upon the type of muscle relaxant used. Each group was comparised of 30 patients.

AGE AND SEX DISTRIBUTION

Out of thirty patients in group I, 3 patients were between the age group of 20-30 years, 10 patients in 30-40 years, 5 patients in 50-60 years and 4 patients were in the 60-70 years of age (Table I).

In group II 3 patients in the range of 20-30 years, 9 patients in the range of 30-40 years, 9 patients were in the age group of 40-50 years, 4 patients were 50-60 years and 5 patients were between the 60-70 years of age (Table-I).

TABLE - I

SHOWING THE AGE DISTRIBUTION OF THE PATIENTS

Age in years	Group I Vecuronium		Group II Pancuronium		Group III Gallamine	
	No.of Patients	%	No.of Patients	%	No.of Patients	%
20-30	3	10	3	10	2	7
30-40	10	33	9	30	5	17
40-50	8	27	9	30	12	40
50-60	5	17	4	13	7	23
60-70	4	13	5	17	4	13
Total	30	100	30	100	30	100

In group III out of 30 patients 2 patients were between the age group of 20-30 years, 5 patients were 30-40 years, 12 patients were 40-50 years, 7 patients were 50-60 years and 4 patients were in age group of 60-70 years (Table I).

TABLE - II

SHOWING SEX DISTRIBUTION OF THE PATIENTS

Sex	Group I Vecuronium		Group II Pancuronium		Group III Gallamine	
	No.of Patients	%	No.of Patients	%	No.of Patients	%
Male	18	60	16	53	11	37
Female	12	40	14	47	19	63
Total	30	100	30	100	30	100

In the present study 45 patients were male while remaining 45 were female. In group I the male female ratio was 18:12. In group II and III this ratio was 16:14 and 11:19 respectively (Table II).

TABLE - III

SHOWING THE WEIGHT DISTRIBUTION OF THE PATIENTS

Weight in Kg.	Group I Vecuronium		Group II Pancuronium		Group III Gallamine	
	No.of Patients	%	No.of Patients	%	No.of Patients	%
40-50	6	20	5	17	9	30
50-60	15	50	15	50	16	53
60-70	6	20	7	23	3	10
70-80	3	10	3	10	2	7
Total	30	100	30	100	30	100

Among the total of 30 patients in group I, 6 patients (20%) were in weight group of 40-50 kg, 15 patients (50%) in 50-60 kg., 6 patients (20%) in 60-70 kg. and 3 patients (10%) in the 70-80 kg of weight group (Table III).

In group II 5 patients (17%) were between 40-50 kg. of weight 15 patients (50%) were between 50-60 kg., 7 patients (23%) were between 60-70 kg and 3 patients (10%) were between the 70-80 kg of body weight (Table III).

Out of 30 patients in group III 9 patient (30%) were in the weight group of 40-50 kg., 16 patients (53%) in the 50-60 kg., 3 patients (10%) in the 60-70 kg and 2 patients (7%) in the weight group of 70-80 kg. (Table III).

TABLE - IV

SHOWING THE VARIOUS TYPE OF SURGICAL PROCEDURES

Surgical Procedures	Group I Vecuronium	Group II Pancuronium	Group III Gallamine
Choledocholithotomy and Cholecystectomy	-	5	4
Appendicectomy	6	4	3
Herniorrhaphy and Herniotomy	4	2	3
Oophorectomy	6	3	5
Abdominal Hystrectomy	3	8	14
Thyroidectomy	3	3	-
Elective Caesarean Section	4	2	1
Urological	4	3	-
	30	30	30

Table IV shows the types of operation in which the drugs were used. In Vecuronium group Appendicectomy were performed in 6 patients, Herniorrhaphy and Herniotomy in

4 patients, Oepharectomy in 6 patients, Abdominal Hystrectomy in 3 patients Thyroidectomy in 3 patients, Elective Caesarean section in 4 patients and Urological operation were in 4 patients (Table IV).

In group II Pancuronium was used to facilitate for Cholecystectomy and Choledocholithotomy in 5 patients. Appendicectomy in 4 patients, Herniorrhaphy and Herniotomy in 2 patients, Oopherectomy in 3 patients, Abdominal Hystrectomy in 8 patients, Thyroidectomy in 3 patients, Elective Caesarean Section in 2 patients and Urological operation in 4 patients (Table IV).

In group III muscle relaxation was provided with Gallamine for Cholecystectomy in 4 patients, Appendicectomy in 3 patients, Herniorrhaphy and Herniotomy in 3 patients, Oopherectomy in 5 patients, Abdominal Hystrectomy in 14 patients and Elective Caesarean Section in 1 patient (Table IV).

TABLE - V

SHOWING CHANGE IN PULSE RATE FOLLOWING THE ADMINISTRATION OF MUSCLE RELAXANTS

Change in Pulse Rate Beat/Min.	Group I Vecuronium		Group II Pancuronium		Group III Gallamine	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
No change	24	80	9	30	-	-
Rise 0-10	6	20	14	46	6	20
Rise 10-20	-	-	5	17	12	40
Rise 20-30	-	-	2	7	9	30
Rise 30-40	-	-	-	-	3	10
Total	30	100	30	100	30	100

PULSE RATE

In Vecuronium group there was no change observed in 80% of patients while in slightly rises (0-10 beats/min.) was recorded in 20% of patients (Table V).

No change in pulse rate was recorded in 30% of patients in Pancuronium group. 70% of patients in this group showed rises in pulse rate. The range was 0-10 beats in 46 percent, 10-20 beats in 17 percent, and 20-30 beats in 7 percent of patients (Table V).

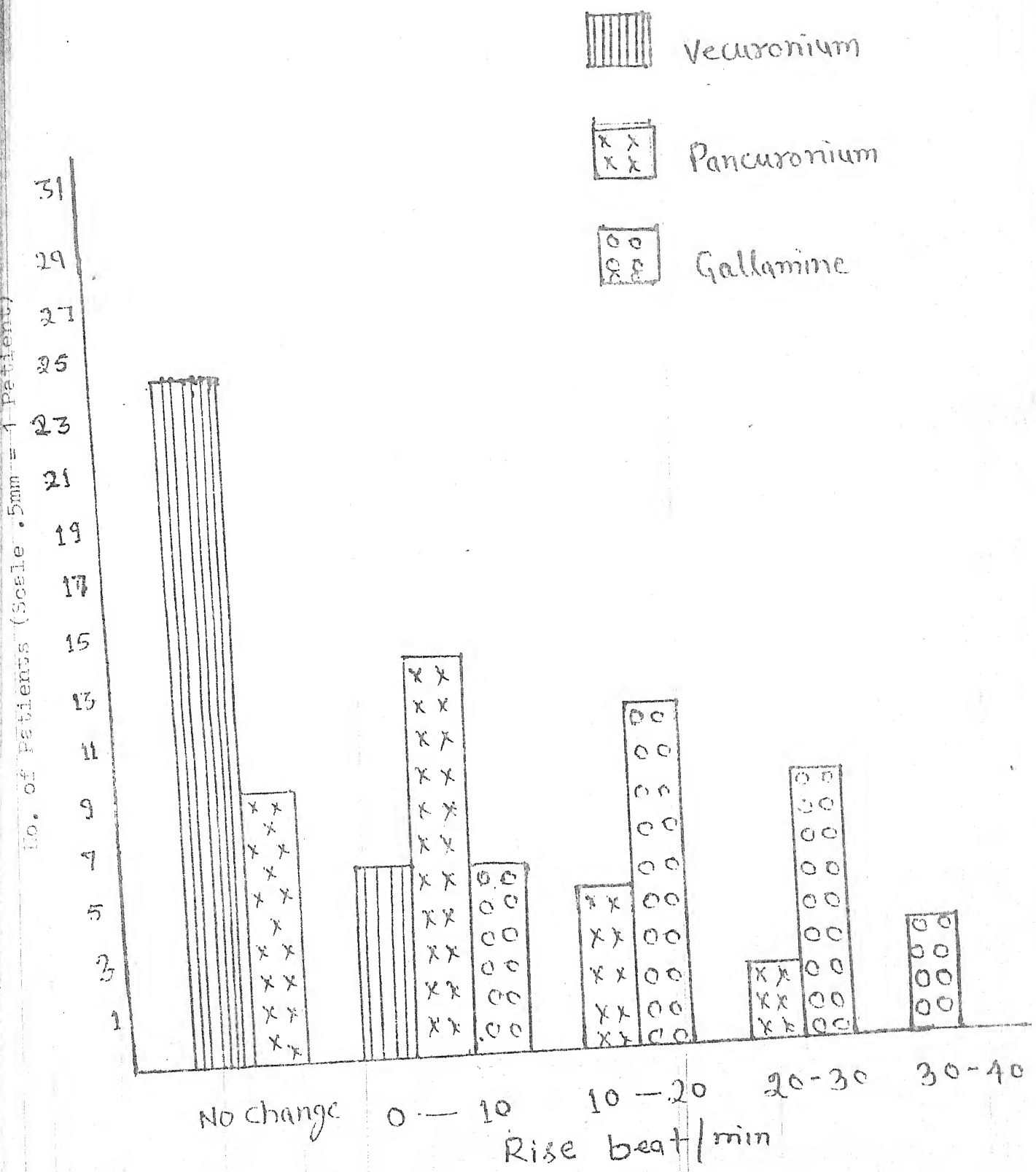

Diagram I - Showing Changes in Pulse rate, after administration of muscle relaxants.

Patients received Gallamine showed marked rise in pulse rate. The rise in pulse rate ranging from 0-10 beats in 20% of patients, 10-20 beats in 40 percent, 20-30 beats in 30 percent and 30-40 beats per minute in 10 percent of the patients (Table V).

TABLE - VI

SHOWING CHANGE IN BLOOD PRESSURE RANGE FOLLOWING THE ADMINISTRATION VECURONIUM

Change in Blood Pressure mm Hg	Systolic Blood Pressure		Diastolic Blood Pressure	
	No.of Patients	%	No.of Patients	%
No change	25	83	26	87
Rise 0-10	5	17	4	13
Rise 10-20	-	-	-	-
Rise 20-30	-	-	-	-
Rise 30-40	-	-	-	-

BLOOD PRESSURE

No change in systolic and diastolic blood pressure was observed in 83% and 87% of patients respectively in Vecuronium group. Slightly rise in blood pressure was recorded in 17% of the patients. The rise in systolic blood pressure in the range of 0-10 mm Hg in 17% of patient while 13% patients showed rise in diastolic blood pressure in this range (Table VI).

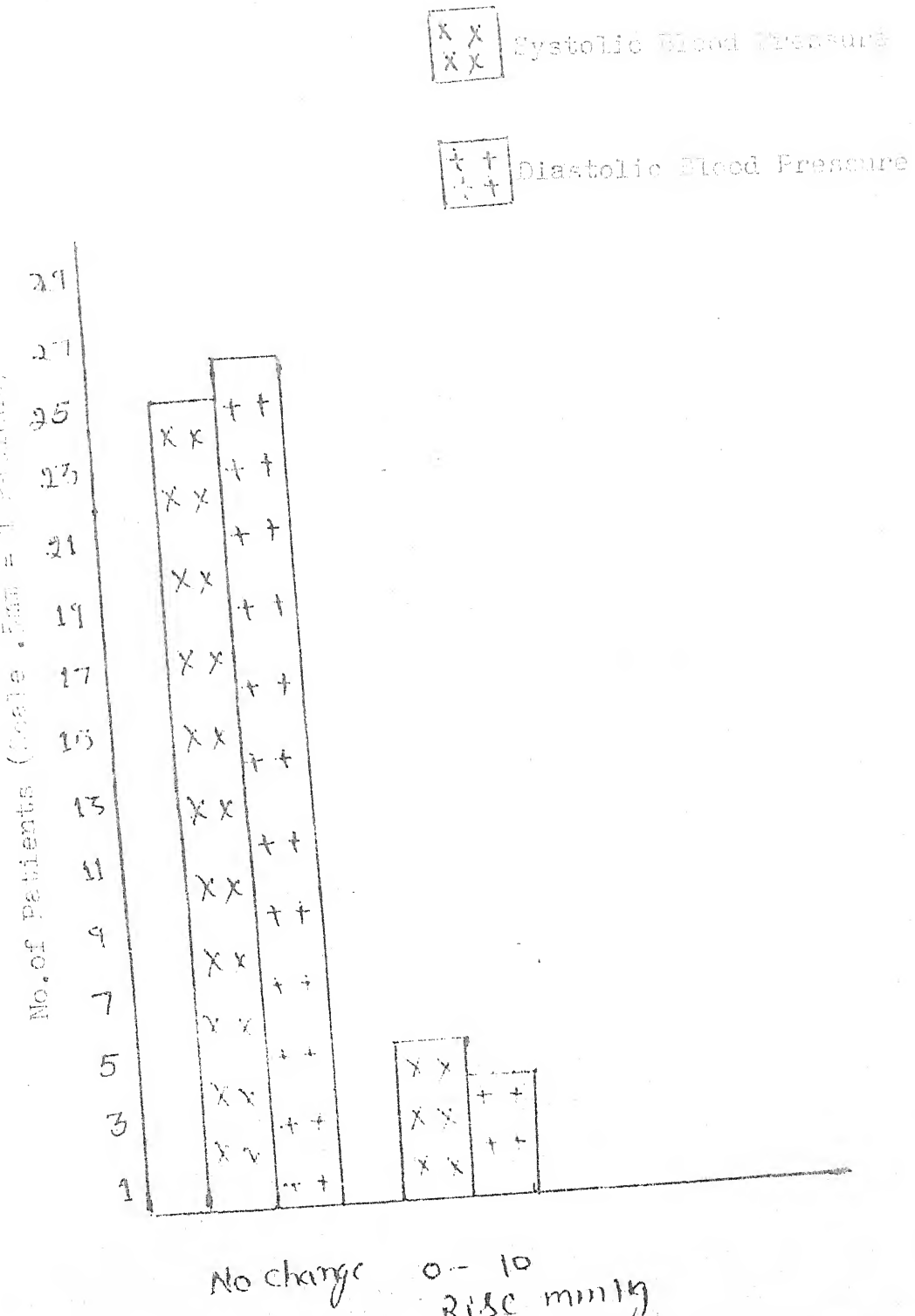

Diagram II - Showing change in Blood Pressure after administration of Vecuronium

TABLE - VII

SHOWING BLOOD PRESSURE RANGE FOLLOWING THE ADMINISTRATION OF PANCURONIUM

Change in Blood Pressure mm Hg	Systolic Blood Pressure		Diastolic Blood Pressure	
	No.of Patients	%	No.of Patients	%
No change	12	40	12	40
Rise 0-10	8	27	9	30
Rise 10-20	6	20	7	23
Rise 20-30	4	13	2	7
Rise 30-40	-	-	-	-
Total	30	100	30	100

In Pancuronium group 40 percent patient had no change in Systolic and diastolic blood pressure while rise in blood pressure was observed in 60 percent of the patient. The rise in systolic blood pressure was in the range of 0-10 mm Hg in 27 percent of the patients, 10-20 mm Hg in 20 percent and 20-30 mm Hg in 13 percent of the patients. The rise in diastolic blood pressure was observed in the range of 0-10mm Hg in 30% of the patients, 10-20 mm Hg in 23% and 20-30 mm Hg in 7% of the patients (Table VII).

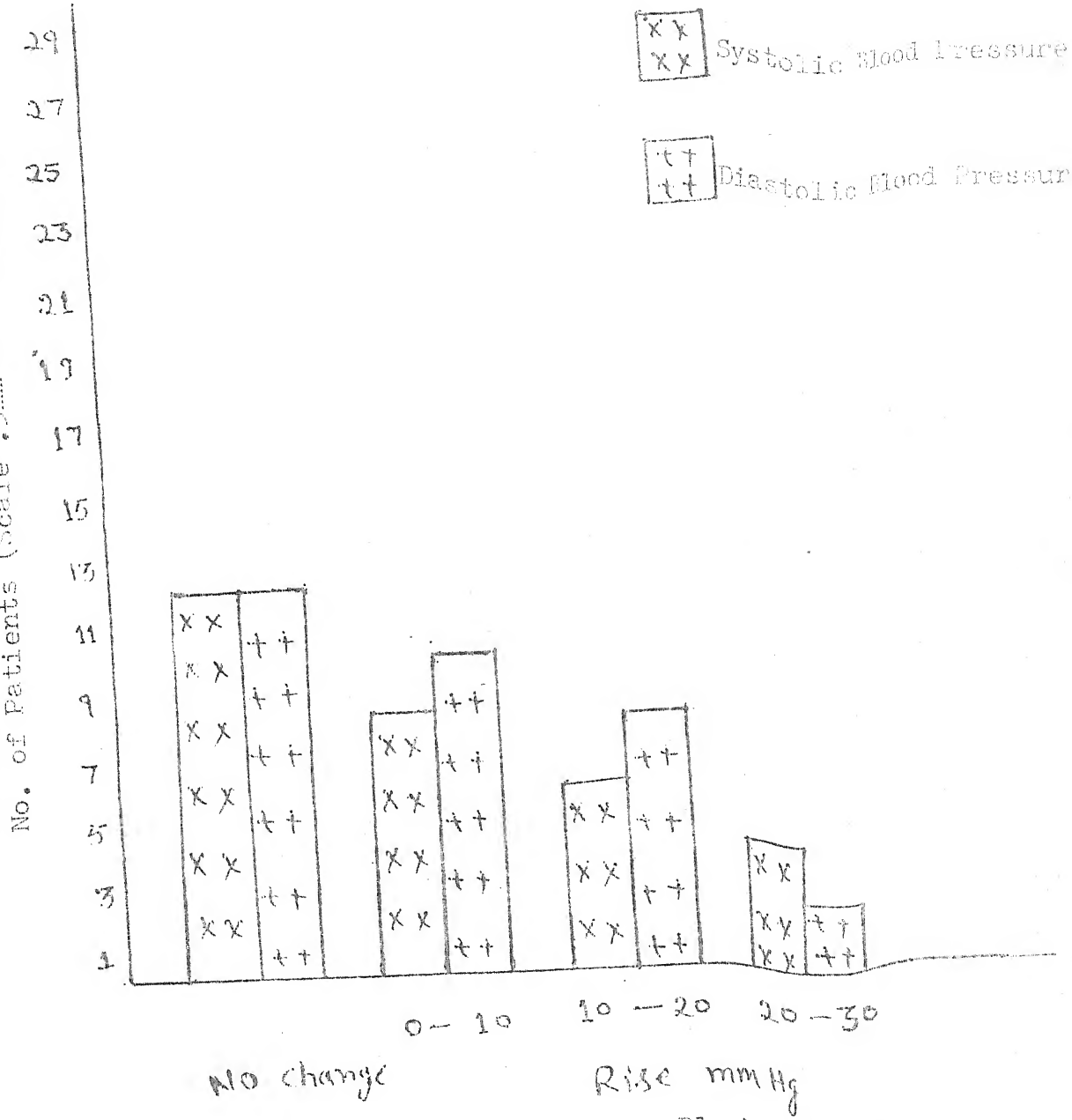

Diagram III - Showing changes in Blood Pressure, after administration of Pancuronium

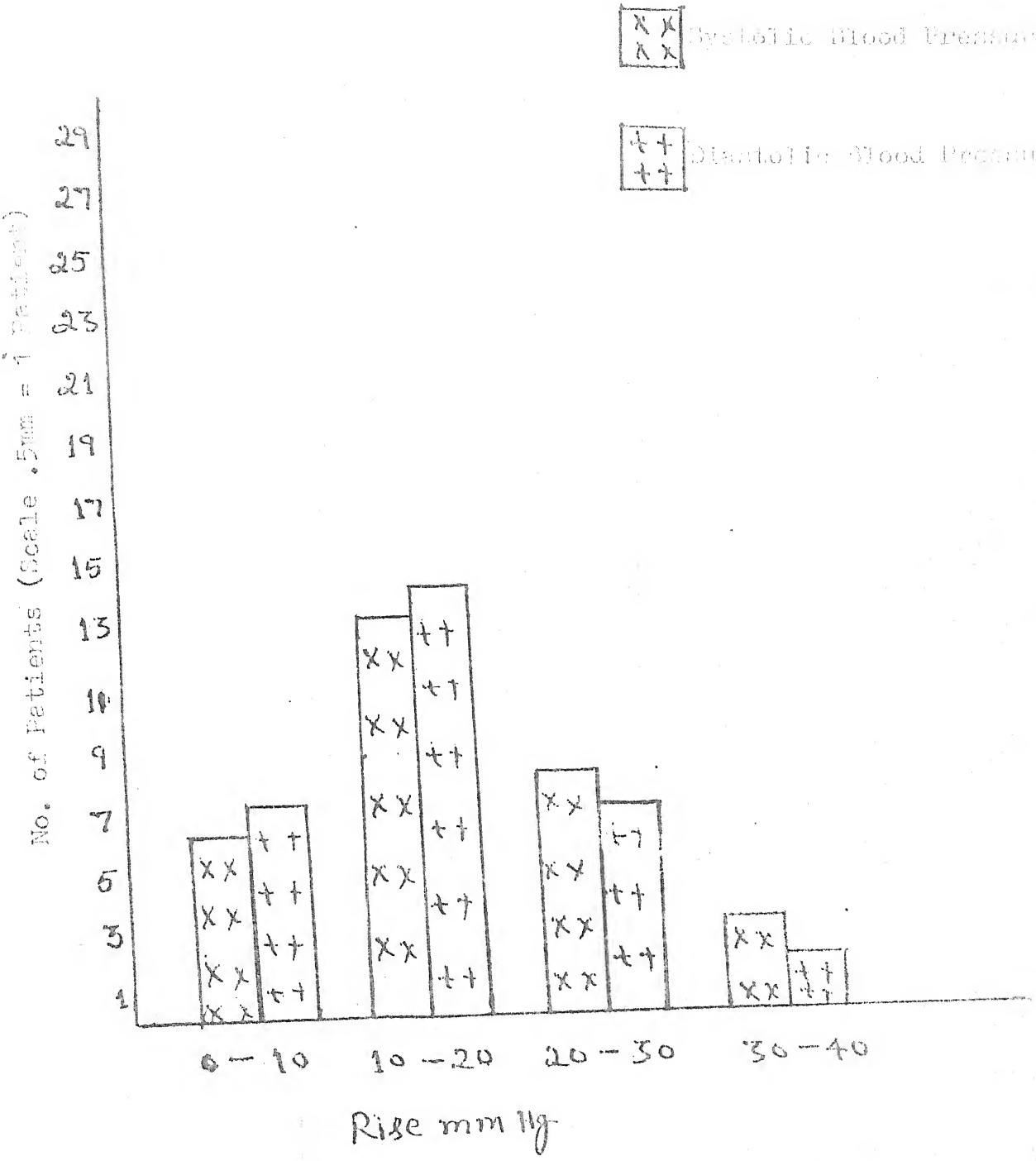

Diagram IV - Showing changes in Blood Pressure after administration of Gallamine

TABLE - VIII

SHOWING THE CHANGE IN BLOOD PRESSURE RANGE FOLLOWING THE ADMINISTRATION OF GALLAMINE

Change in Blood Pressure mm Hg	Systolic Blood Pressure		Diastolic Blood Pressure	
	No.of Patients	%	No.of Patients	%
No change	-	-	-	-
Rise 0-10	6	20	7	23
Rise 10-20	13	43	14	47
Rise 20-30	8	27	7	23
Rise 30-40	3	10	2	7
	30	100	30	100

Marked rise in blood pressure was recorded in all the patients of Gallamine group. Rise in systolic blood pressure was ranging from 0-10mm Hg in 25 percent of the patients, 10-20 mm Hg in 43 percent, 20-30 mm Hg in 27 percent and 30-40 mm Hg in 10 percent of the patients, while rise in diastolic blood pressure was in the range of 0-10 mm Hg in 23 percent of the patients, 10-20 mm Hg in 47 percent, 20-30 mm Hg in 23 percent and 30-40 mm Hg in 7 percent of the patients (Table VIII).

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DISCUSSION

DISCUSSION

Muscle relaxants are among the most commonly employed drugs in the anaesthetic practice. It become possible to produced active muscular relaxation without unwanted effects on various systems of the body, with the help of these druga. Muscle relaxants are required during various surgical procedures particularly in the thoracic and abdominal operations. These agents also made it possible for the anaesthesiologist to have adequate required control over the ventilation of the patients.

The present study was profound to evaluate the efficacy of nondepolarising muscle relaxants. Vecuronium, Pancuronium and Gallamine on Cardiovascular system.

In the present study only adult patients were selected. Their age ranged between 20 to 65 year to circumvent the variables at the extrems of age. Patients subjected to routine surgical procedures were included in this study and emergency surgical

procedures were excluded to maintain standarised condition as far as possible. All patients were of ASA grade I or II.

Calton and Brown (1972) reported that the type of premedication had no effects on dose requirement of relaxants, while Macdowell and Clarke (1969), Pandit and Dundee (1970), Magbagbeola (1972) administered a standard premedication. Atropine and Pethidine were used in this study as a premedication in all patients of each group. Mrs. Bhargawa et al. (1977) also given Pethidine and Atropine as a premedication in their study.

In this study, same premedicant drugs, induction agents, and supplementary analgesia drugs were used in all cases to avoid the influence on the dosage and action of muscle relaxant drugs.

The present study shows that Vecuronium was found to most effective in possessing the Cardiovascular stability. The doses used in this study were recognized as being only approximately equipotent since most previous authors had found Vecuronium to be a little more potent than Pancuronium (Baird and Read 1980, Krieg, Crul and Beelj 1980, Vibymoqensen, Jorgensen

et al. 1980, Fahey et al. 1980 and Kerr et al (1982).

In this group 80% patient had no change in pulse rate. 83% and 87% of the patient had no change in systolic and diastolic blood pressure respectively, while only 20% patient showed slight rise (up to 10 beat/minute) in pulse rate. A little rise in systolic blood pressure was observed in 17% cases and 13% patient showed a minimal rise in diastolic blood pressure. These changes were not clinically significant. Our finding regarding heart rate and arterial blood pressure changes in fit adult patients after Vecuronium substantiate similar findings reported by other observers, Crul and Booij (1980), Booij et al. (1980), Gregoretti et al. (1982), Engback et al. (1983), Bhatia et al. (1985), and Ferres et al. (1984).

Lavery et al. (1986) found that in healthy patients under carefully control condition, Vecuronium showed no significant changes in heart rate, systolic, diastolic and mean arterial blood pressure reduced significantly ($P<0.05$) 3-5 minute after Vecuronium administration. However by 30 minute the diastolic blood pressure was significantly greater than control. These occure with Halothane anaesthesia Robertson et al.

(1983) was recorded a statistically significant decrease in heart rate (4-5%) and was not consitered clinically significant. The similar alteration was noted by Barnes et al. (1963). Animal experiment have shown that in contrast to Pancuronium and other nondepolarising muscle relaxants, Vecuronium in doses 20 times greater than these required for neuromuscular blockade, has no effect on the heart rate, arterial blood pressure or the sympathetic nervous system. Marshall et al. (1980), Fitzal et al. (1983). Agarwal et al. (1969) observed significantly elevation is mean pulse rate and mean arterial blood pressure during intubation which settled after 10 minute to a level above the preinduction level.

Vecuronium, being devoid of autonomic neural activities, does not produced any cardiovascular effects, Marshall et al. (1980), Booij et al (1980), Gregoretti et al. (1982) and Engback et al. (1983). Since Atropine was given before induction, patients had a tachycardia initially and consequently, the reasons for these changes in heart rate may be complex Norvik et al. (1988).

Considering the haemodynamic effects, the patients who received Pancuronium shows rise in pulse rate and blood pressure. The rise in pulse rate was the tune of 70%, while the blood pressure went up by

60% of the patients. In the same group 30% and 40% of the patients showed no change in pulse rate and blood pressure respectively. Slightly rise in blood pressure was observed in 30% of the patients while other 30% patients showed moderate rise in blood pressure. These results are comparable to the observation of Baird (1968), Medowell and Clark (1969) Levin (1971), Bennett et al. (1973), Mrs. Bhargwe Engback et al. (1983), Baijal et al. (1990) and Singh et al. 1990.

Previous studies of the effects of Pancuronium on heart rate and arterial blood pressure in man have been conflicting. Baird and Reid (1967) found that it had little effect on arterial blood pressure and heart rate, Medowell and Clark (1969) showed that it had little effect on heart rate and caused a slight, and statistically insignificant, fall of arterial blood pressure, conversely Loh (1970) found that in a dose of .12mg/kg. Pancuronium caused increases of both heart rate and mean arterial blood pressure. Kelman and Kennedy (1971) observed that in a dose of 0.07mg/kg body weight, Pancuronium caused marked and statistically significant increase of heart rate accompanied by lesser, but still statistically significant

increases of mean arterial blood pressure. Barnes et al. (1982) showed that, when Pancuronium was used in clinical practice the tachycardia would be marked in the presence of vagal blockade and increase in mean arterial blood pressure did not appear to correlate with the increase of heart rate.

The most likely explanation for this discrepancy is that the cardiovascular actions of Pancuronium due to the release of Catecholamine Komesaroff (1970). The second concept is that it is secondary to the vagolytic action of the drug. Animal studies by Benta, Goorisean and Derkre (1968) suggested that Pancuronium reduces the effects of vagal stimulation on the heart, it might therefore be expected to cause on increase of heart rate. Duke et al. (1973) have shown that Pancuronium exerts its cardiovascular effects primarly by blocking muscaranic receptores in the heart. Hughes and Chapple (1976) proved in cats that Pancuronium caused blocked at vagal post ganglionic sites in the heart an activity correlated well with the known liability of mild hypertension and tachycardia in man.

In the present study Gallamine was found to be most potent drug regarding to produced adverse effects over haemodynamic status of the patient.

The tachycardia which follows after administration of gallamine triethiodide was marked in both degree and rapidity of onset, and in the present series the average increase in the rate was up to 40 beat per minute, which was accordance to Kennedy and Farman (1968). Tachycardia was said to occur however small the dosage of Gallamine triethiodide Doughty and Wylie (1951).

Marked rise in systolic and diastolic blood pressure was found following administration of Gallamine. The maximum rise in blood pressure in the present series was up to 40mm Hg, which was comparable to Doughty and Wylie (1951), Kennedy and Farman (1968), Burnall et al. (1970), Hissle et al. (1971), Stoelting (1973).

Sheth and Sabina (1980) was observed no change in pulse rate in 32% and blood pressure in 36% of the patient while increases in pulse rate and blood pressure was recorded in 68% and 64% of the patient respectively.

Joshi and Ghosh (1981) have beem observed no change in pulse rate in 14% of the patient while in 84% it was increased and 2% showed decrease in pulse rate. Fall in blood pressure was observed in 15%, no change in 36% and rises in 46% of the patient after administration of Gallamine.

The cardiovascular effects of the gallamine triethiodide has been believed to result from blockade of the muscarinic effects of acetylcholine liberated from the post ganglionic vagal nerve endings (Riker and Wescoe 1951). In this action, the drug resembles atropine, although it is much weaker (Laity and Garg 1962), but remarkably it exhibits this atropine like effect at no other site (Paton 1959). Neither is there any evidence of general sympathetic stimulation (Wein 1951) and the effects on Preganglionic sympathetic nerves are minimal (Millar and Biscoe 1965). A direct stimulant effect on intracardiac Beta receptors has been demonstrated (Morgenstern and Splinth 1965, Lee and Atkinson 1973).

Reversal with 12mg Atropine and 2.5mg Neostigmine was found to be adequate in all the cases in three groups as judged clinically. Baird (1968) reported that if reversal was attempted within 30 minute of the last dose, results were less than ideal in case of Pancuronium.

Wood Smith et al. (1973) reported that when a full paralysing dose of relaxant was still present at the end of operation, Gallamine in fact was more difficult to reverse with Neostigmine with equipotant dose of Pancuronium. Reason for this was beyond of explanation.

Baijal et al. (1990) was observed that 40% of the patient received Vecuronium, required no reversal.

CONCLUSION

From the present study we concluded that in comparision with Pancuronium and Gallamine, the Vecuronium represents a remarkable step toward the "Ideal muscle relaxant". Regarding Cardio-vascular stability.

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